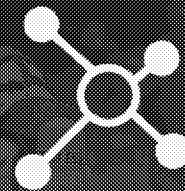




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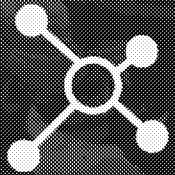
Presenter: Leslie Cadet, MD
Occupational & Environmental Medicine
lcadet@hsph.harvard.edu



MILITARY FIREFIGHTER EXPOSURE TO PERFLUOROALKYL SUBSTANCES (PFAS) AND ADVERSE REPRODUCTIVE OUTCOMES



Discussant: Carmen Messerlian, PhD
Department of Environmental Health
cmesser@hsph.harvard.edu



OBJECTIVES

1

Define perfluoroalkyl substances (PFAS), describe common sources and routes of exposure, and understand why PFAS are used in firefighting foam

2

Briefly explain the toxicological and human literature on PFAS exposure and male and female reproductive health

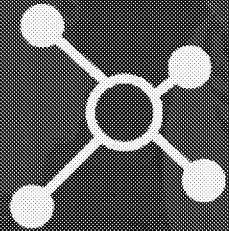
3

Identify the clinical implications of PFAS exposure in a couple attempting conception at Wright-Patterson Air Force Base

4

Discuss the public health implications of PFAS exposure in reproductive aged couples

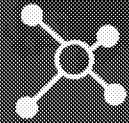




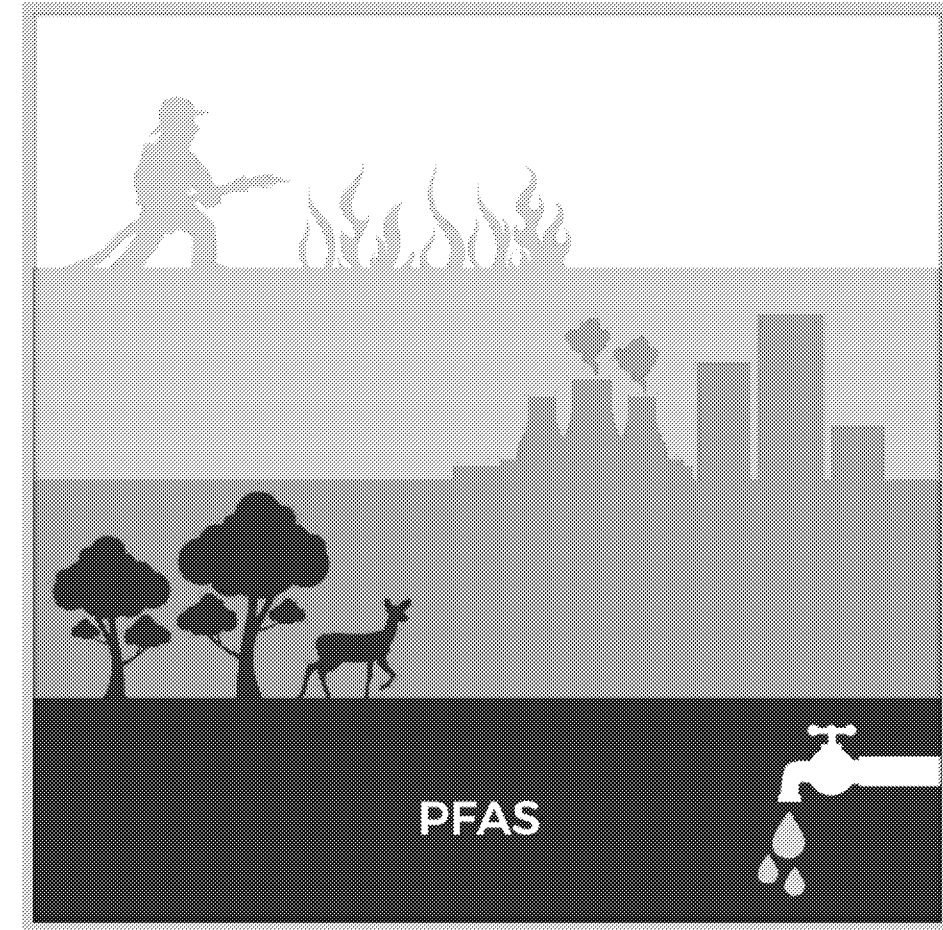
PART-1

UNDERSTANDING PERFLUOROALKYL SUBSTANCES

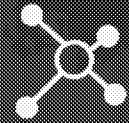
What are Perfluoroalkyl Substances?



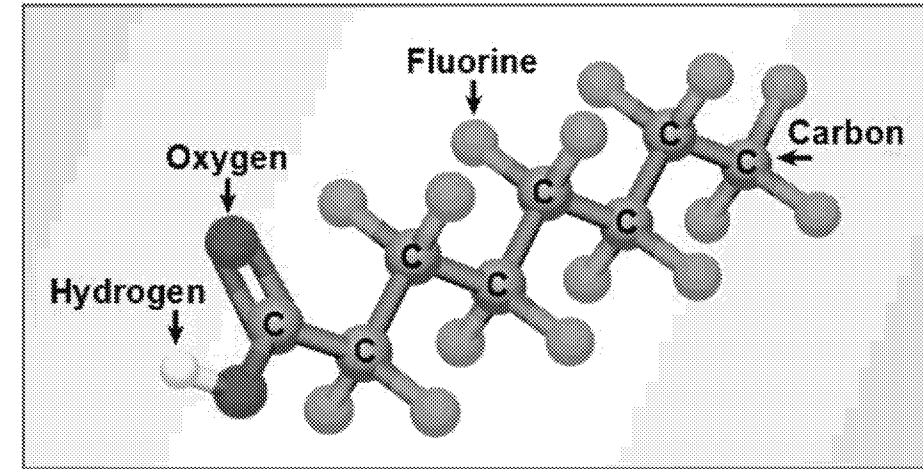
- ✓ Per- and polyfluoroalkyl substances (PFAS) are a large class of synthetic chemicals
- ✓ Widely used to make products heat, oil, stain, and water resistant
- ✓ In production since 1950s
- ✓ Previously known as perfluorinated chemicals (PFCs)
- ✓ Hundreds of different PFAS exist
- ✓ Perfluorooctyl sulfonate (PFOS) and perfluorooctanoic acid (PFOA) are the two most well-known and well-studied



What are some of the features of PFAS?

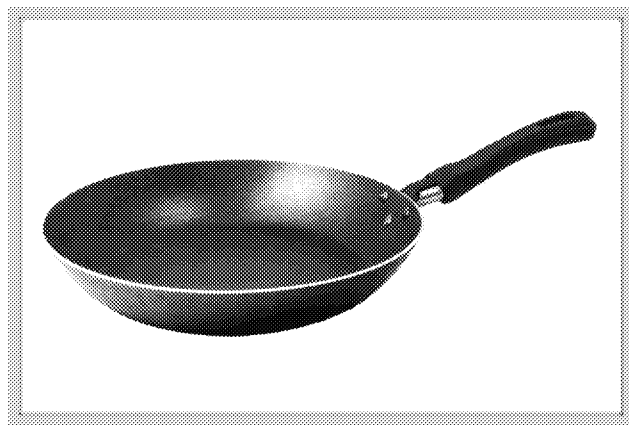
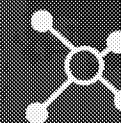


- ✓ All PFAS contain carbon (C) and fluorine (F) atoms
- ✓ C-F bonds: strongest covalent bonds in organic chemistry
- ✓ Properties (and name) change based on the length of the carbon chain in the PFAS molecule
- ✓ PFOA is referred to as C8 because there are 8 carbon atoms in the chain
- ✓ Highly resistant: thermal and chemical stability



PFOA, also known as C8, has 8 carbons.

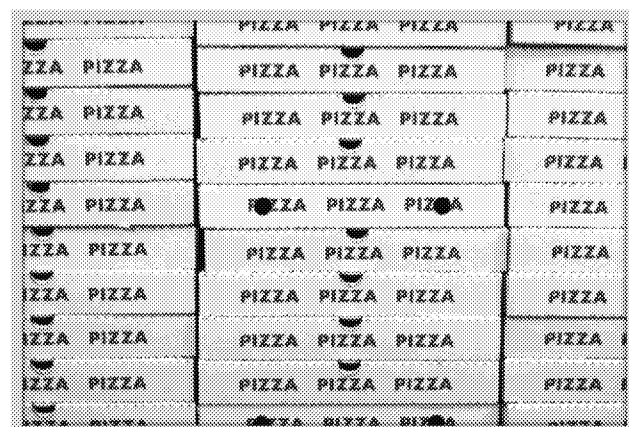
What are some of the common uses of PFAS ?



Non stick cookware
(e.g., Teflon pans)



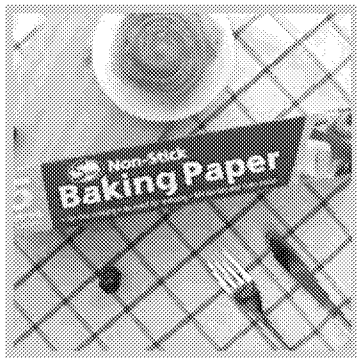
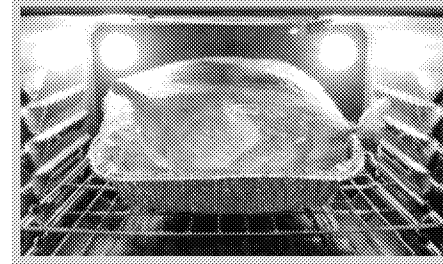
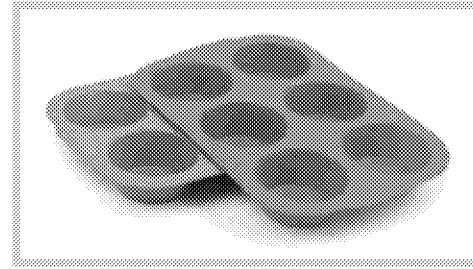
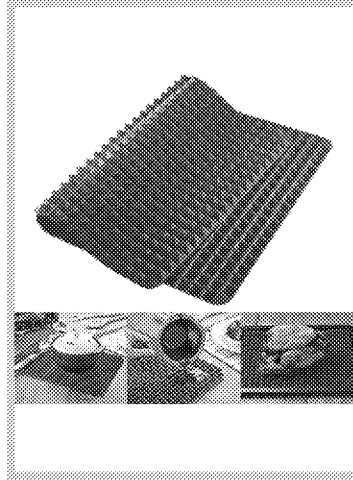
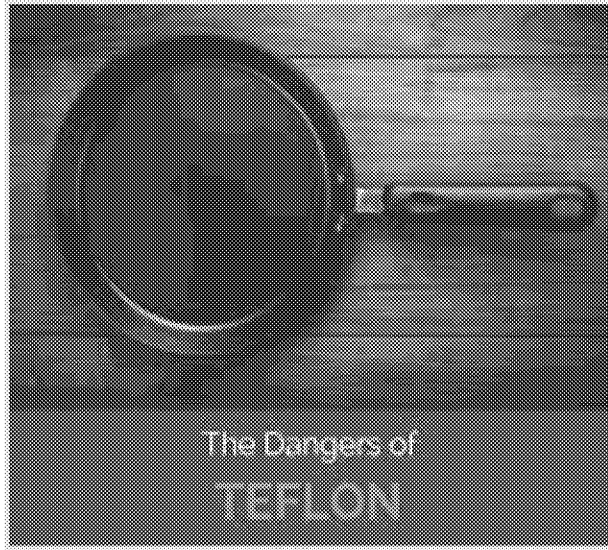
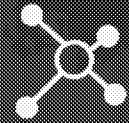
Water and/or stain resistant
carpet, textiles, and clothing
(e.g., Scotchguard)



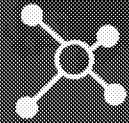
Paper and
cardboard food
packaging
(e.g., pizza boxes,
cooking paper)



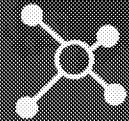
Aqueous Film Forming Foam
(AFFF) Fire Fighting Foam



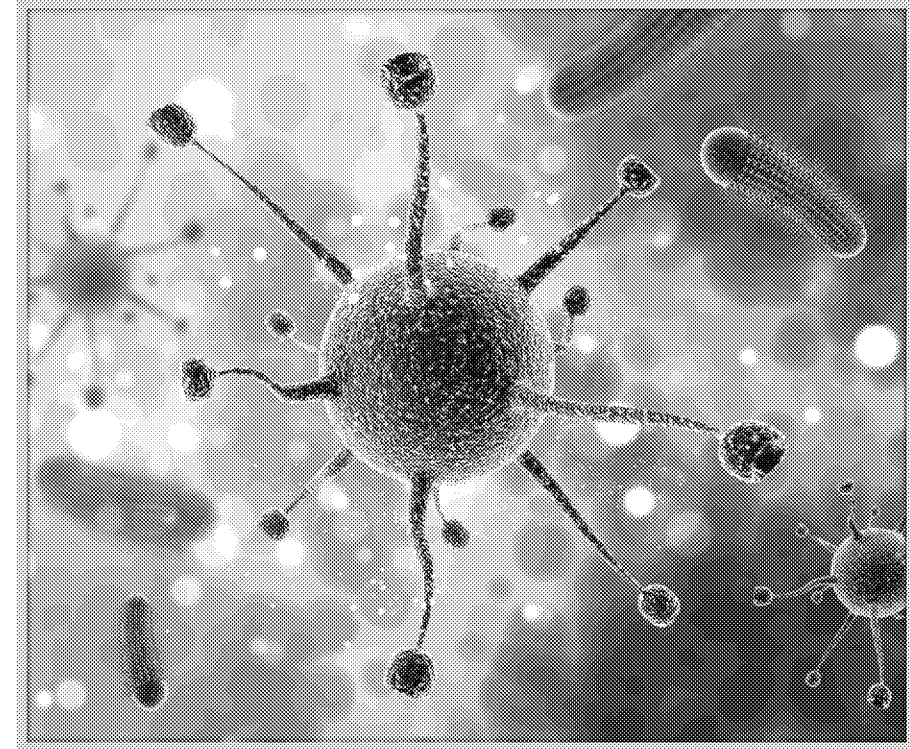
Why are PFAS used in Firefighting Foam?

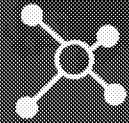


- ✓ Chemical diversity in types of PFAS → multifunctional uses
- ✓ Resist degradation and oxidation → they don't break down
- ✓ Thermal stability primarily attributed to the strength of the C-F bond
- ✓ HIGHLY resistant to heat degradation even at extreme temperatures
- ✓ Some PFAS decompose and mineralize at temperatures >1000 Celsius

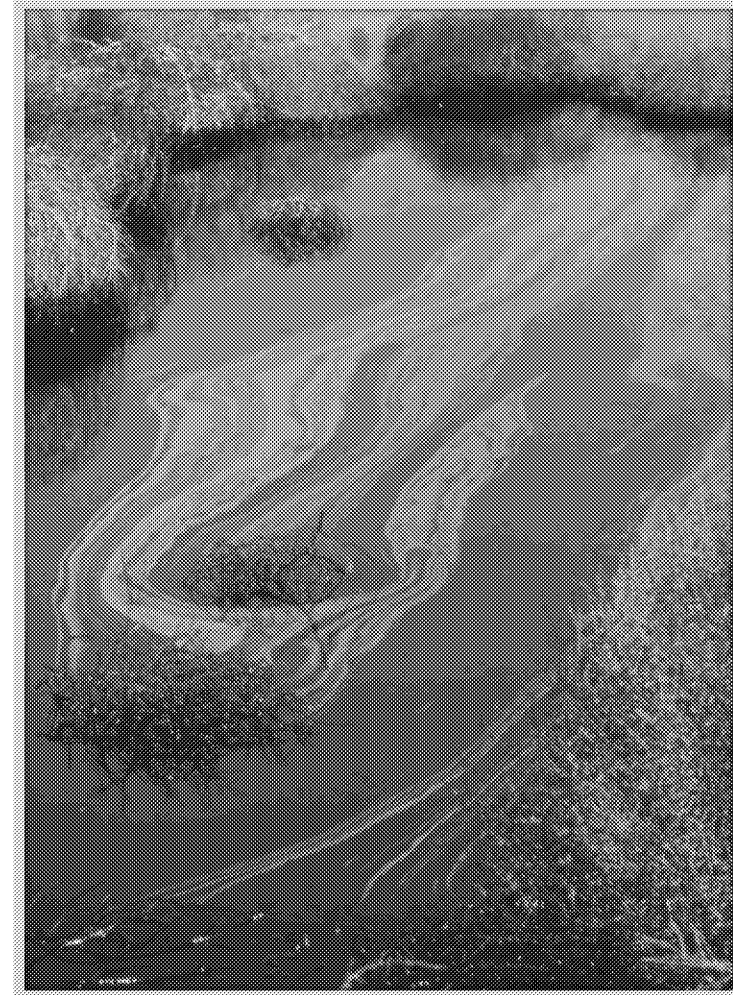


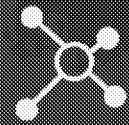
- ✓ Drinking contaminated water: private wells and municipal systems
- ✓ Ingesting contaminated food: food packaging; bioaccumulation of meat and fish; produce grown in contaminated soil and water
- ✓ Hand-to-mouth transfer from surfaces/products: migrate from PFAS consumer goods
- ✓ Inhalation of air and dust: house dust; workplace air exposure
- ✓ Dermal absorption: contact with textiles, clothing, sofa seating, other



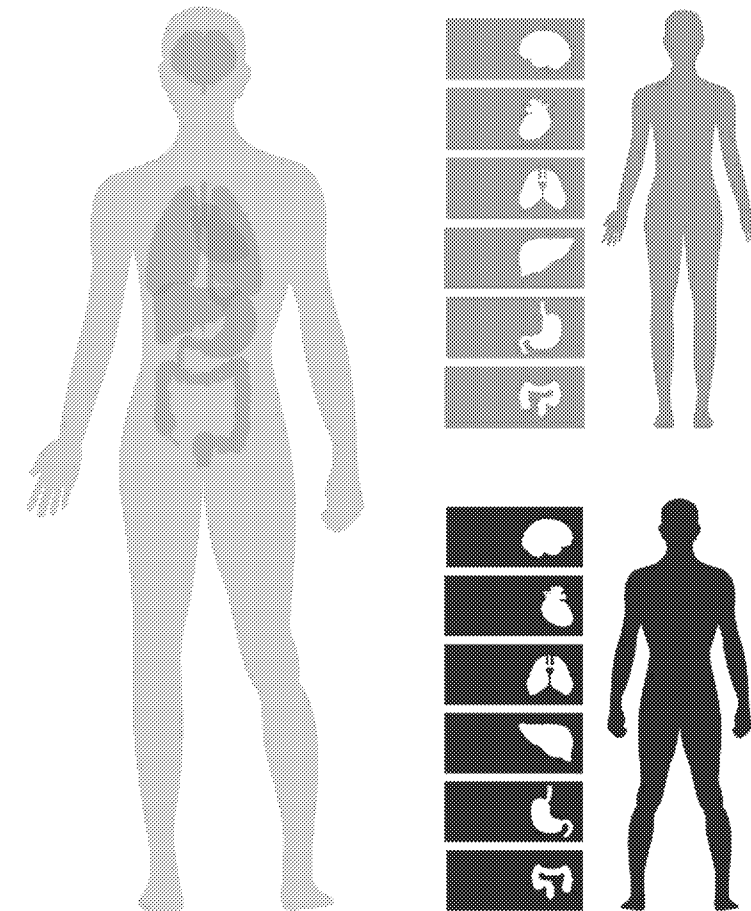


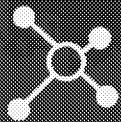
- ✓ Drinking water can be a source of exposure in communities where these chemicals have contaminated water supplies
- ✓ Contamination: localized, usually associated with a specific facility
 - Parkersburg, West Virginia
 - <http://highline.huffingtonpost.com/articles/en/welcome-to-beautiful-parkersburg/>
 - Oil refineries, airfields or other locations used for firefighting





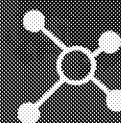
- ✓ Bind to protein molecules in serum upon absorption
- ✓ Bioaccumulate but not in fatty tissue
- ✓ Renal clearance: influenced by GFR, mostly eliminated in urine
- ✓ Short chain PFAS faster clearance than long chain PFAS
- ✓ Variability in accumulation and elimination by sex
- ✓ Detected in: serum, seminal fluid, amniotic fluid, cord blood, breast milk, liver tissue
- ✓ Efficient placental transfer





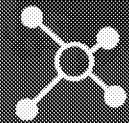
- ✓ Elimination half-life in humans: 2.3 to 8.5 years

PFAS	HALF LIFE
Perfluoroactonoic acid (PFOA)	3.8 years
Perfluorooctanesulfonate (PFOS)	5.4 years
Perfluorohexane sulfonic acid (PFHxS)	8.5 years



PFAS Analytes*	Women 2007-2008 Concentration (µg/l)			
	PERCENTILE			
	GM***	50 th	75 th	95 th
PFOS (Scotchguard)	10.7	10.8	17.2	33.6
PFOA (C8, Teflon)	3.56	3.70	5.20	8.30
PFNA (C9)	1.33	1.30	1.90	3.40
PFHxS (C8)	1.46	1.40	2.60	7.50
PFDA (C10)	0.27	0.30	0.40	0.80

*PFOS, perfluorooctane sulfonate; PFOA, perfluorooctanoate; PFNA, perfluorononanoate; PFHxS, perfluorohexane sulfonate; PFDA, perfluorodecanoate; **Limit of detection (LOD) 0.1 for all analytes except PFHxS (0.2); ***GM, Geometric Mean



- ✓ Concern about the persistence, bioaccumulation, and possible ecological and human health effects of long-chain PFAS led to a voluntary phase-out by manufacturers
- ✓ Short-Chain Regrettable Substitution

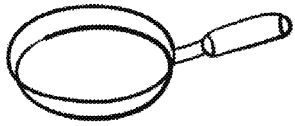
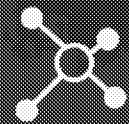
The New York Times ***3M Says It Will Stop Making Scotchgard***

By DAVID BARBOZA MAY 17, 2000

"These products have been safely used for 40 years and they continue to be safe," said William E. Coyne, the head of research and development at 3M. "But the best decision we can make now is to stop adding to the environment. This is a corporate responsibility issue. This product does not decompose, it's inert -- it's persistent; it's like a rock." Officials of 3M said they ran exhaustive tests on animals and humans and found no adverse health effects. But because the compounds were persistent in the environment and in human blood, the company said it alerted regulators and began working to come up with alternative compounds.



Which of the following products do not contain PFAS?



A

Non-Stick Cookware



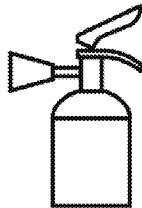
B

Stain-Repellant Upholstery



C

Cellophane Wrap



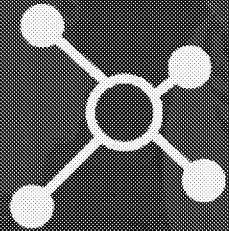
D

Certain fire fighting foams



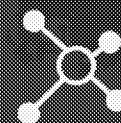
E

Wooden dishware



PART-2

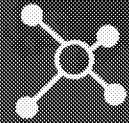
PFAS AND REPRODUCTIVE HEALTH



RODENT ANIMAL MODELS

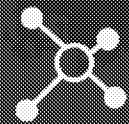
- Reduced testosterone levels
- Reduced pup weight and gestational length
- Increased pup loss (decrease in number of pups born alive)
- Delays in postnatal growth

Fenton, 2009. EFSA, 2008. CDC, 2017



HUMAN: FERTILITY AND PREGNANCY OUTCOMES

- Possible association with longer time to pregnancy, reduced fecundity, and increased risk of pregnancy loss
- Increased risk of pregnancy induced hypertension and pre-eclampsia
- Higher PFOS exposure may be associated with morphologically abnormal sperm and possibly male infertility
- No studies have examined the role of paternal PFAS exposure on pregnancy loss and other birth outcomes

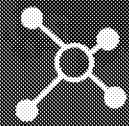


HUMAN: BIRTH OUTCOMES

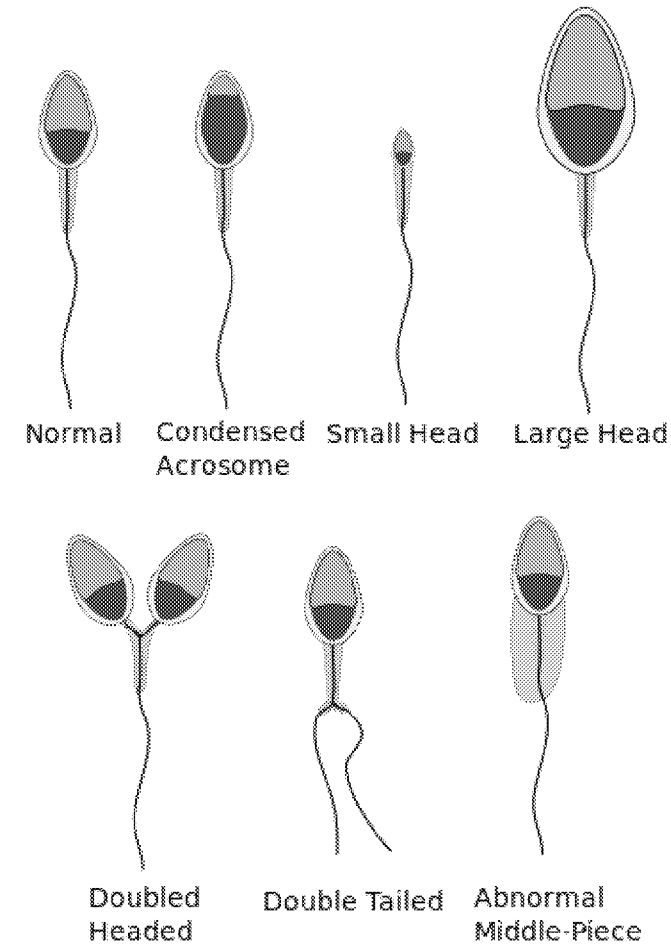
- Decreased birth weight
- Small for gestational age
- Preterm birth

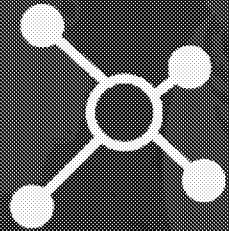
Lauritzen, 2017. Sagiv, 2017

Which of the following is a potential reproductive health effect of PFAS exposure?



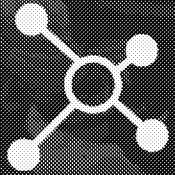
- a) Decreased Antral Follicle Count
- b) Macrosomia (Large Infant)
- c) Stillbirth
- d) Abnormal Sperm Shape





PART-3

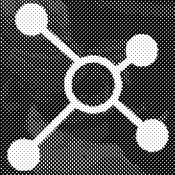
CLINICAL IMPLICATIONS OF PFAS EXPOSURE IN COUPLES ATTEMPTING CONCEPTION



Clinical Vignette

- ✓ 36-year-old nulliparous female TSgt and her husband, 38-year-old TSgt, are referred for an infertility work up.
- ✓ They are both Air Force service members, and have worked in the Civil Engineering Squadron as fire fighters since their enlistment at the ages 18 and 20, respectively.
- ✓ They have tried unsuccessfully for two years to conceive.

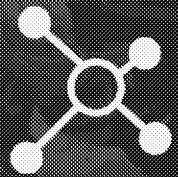




Clinical Vignette

- ✓ There has been much discussion over the last two years within their squadron, regarding the Air Force's uses of PFOA and PFOS
- ✓ Ground water at Wright Patterson Air Force Base in Dayton, OH has been contaminated
- ✓ The couple wonders if this, and similar exposures over the last 15 years, has lead to their infertility problems

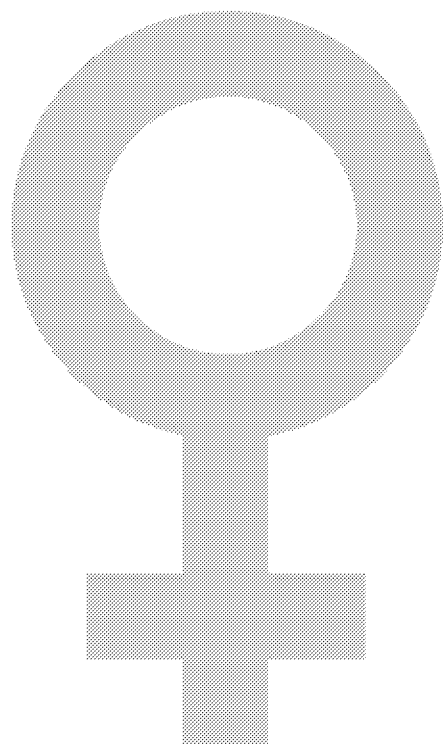
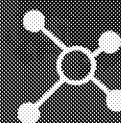




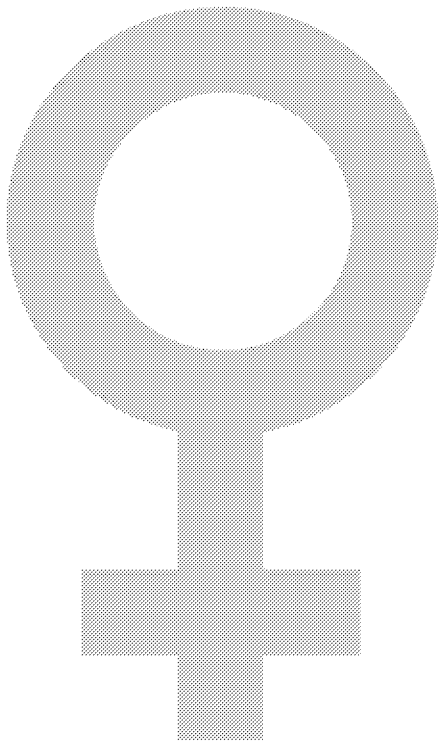
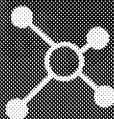
Live Fire Training Exercise



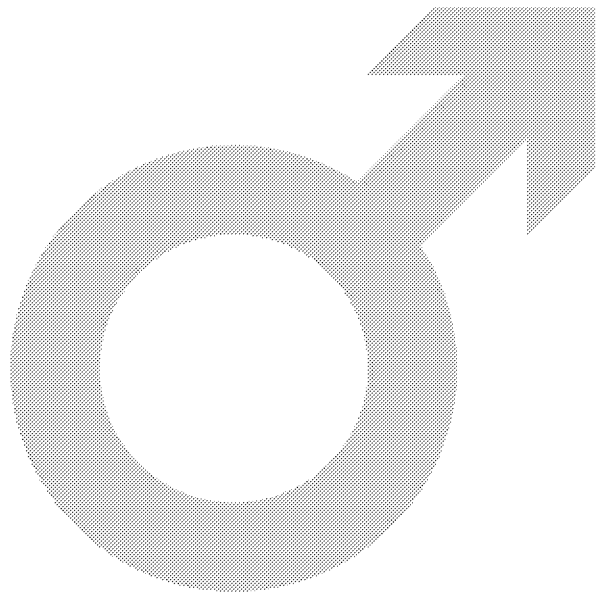
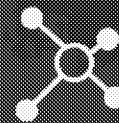
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FSH – Day 3	12 IU/L
LH	10 IU/L
AMH	1.2 ng/ml
Prolactin	20 ng/dl
Progesterone	0.9 ng/ml
AFC – Day 3	5 (Left), 4 (Right)
TSH, T4, TPO-Antibodies	2.8 mIU/L, 6 ug/dl, Antibody-negative

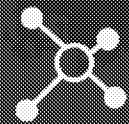


PFOA	8 ug/ml (NHANES, 2009: ref mean 3.56)
PFOS	33 ug/ml (NHANES, 2009: ref mean 10.7)
Hysterosalpingograph	Within Normal Limits
Transvaginal U/S	Uterus and ovaries have a normal appearance



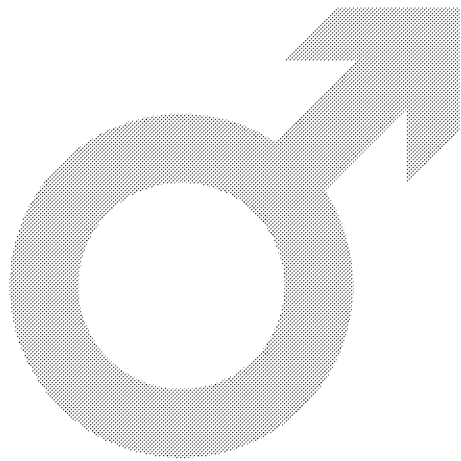
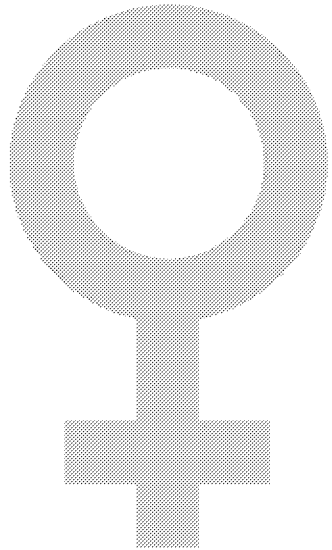
Testosterone	700 ng/dl
FSH	3 mIU/mL
PFOA	7 ug/l (NHANES, 2009: ref mean 4.47)
PFOS	34 ug/l (NHANES, 2009: ref mean 23.2)

Is the semen analysis normal?



✓ Yes

✓ No



Volume, 2.2 ml

Appearance, normal

Morphology

✓ 23% normal

✓ 72% head defect

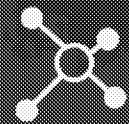
Count

✓ 30 million/ml

Motility

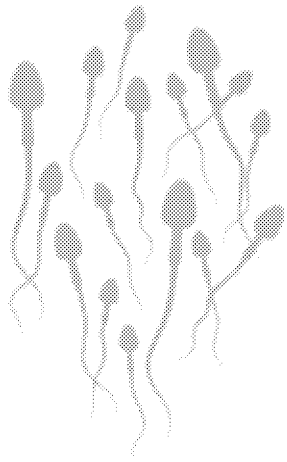
✓ Rapid Progression, 27%

✓ Immotile, 30%

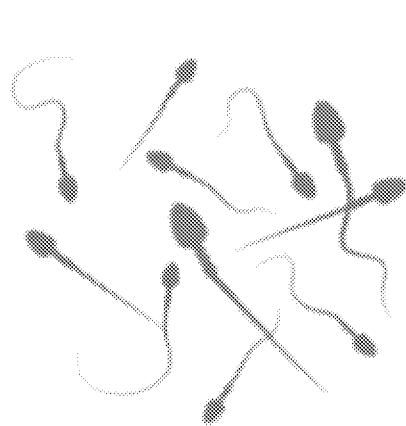


SEMEN ANALYSIS

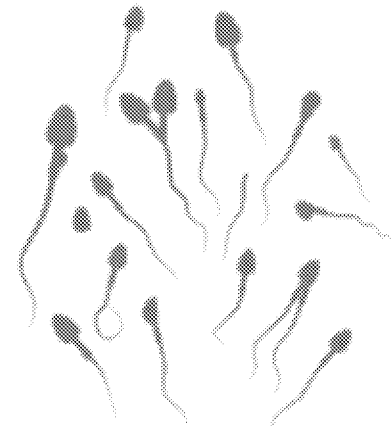
NORMAL RESULTS



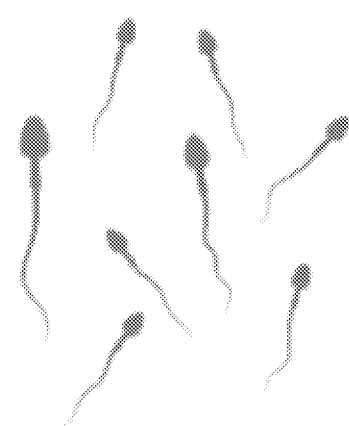
ABNORMAL RESULTS



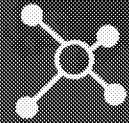
MOTILITY
<40%



MORPHOLOGY
>4%

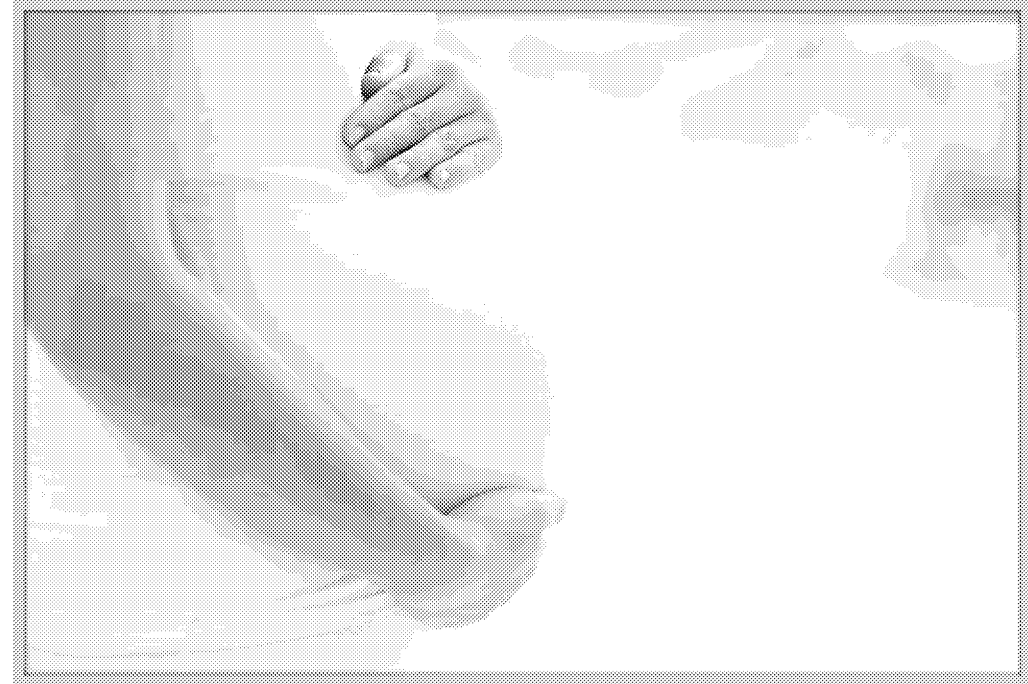


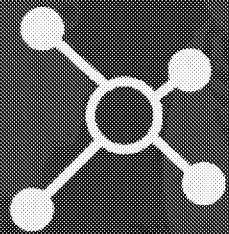
CONCENTRATION
<15 million/ml



HOW WILL THEIR EXPOSURE TO PFAS AFFECT THE PREGNANCY?

- a) There is a need to monitor blood pressure more often during the pregnancy
- b) Health effects of PFAS are specific and cannot be caused by other factors
- c) There is an association with PFAS and pre-eclampsia
- d) Pregnancy induced hypertension occurs in many pregnancies and the specific etiology is often known

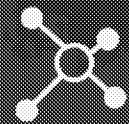




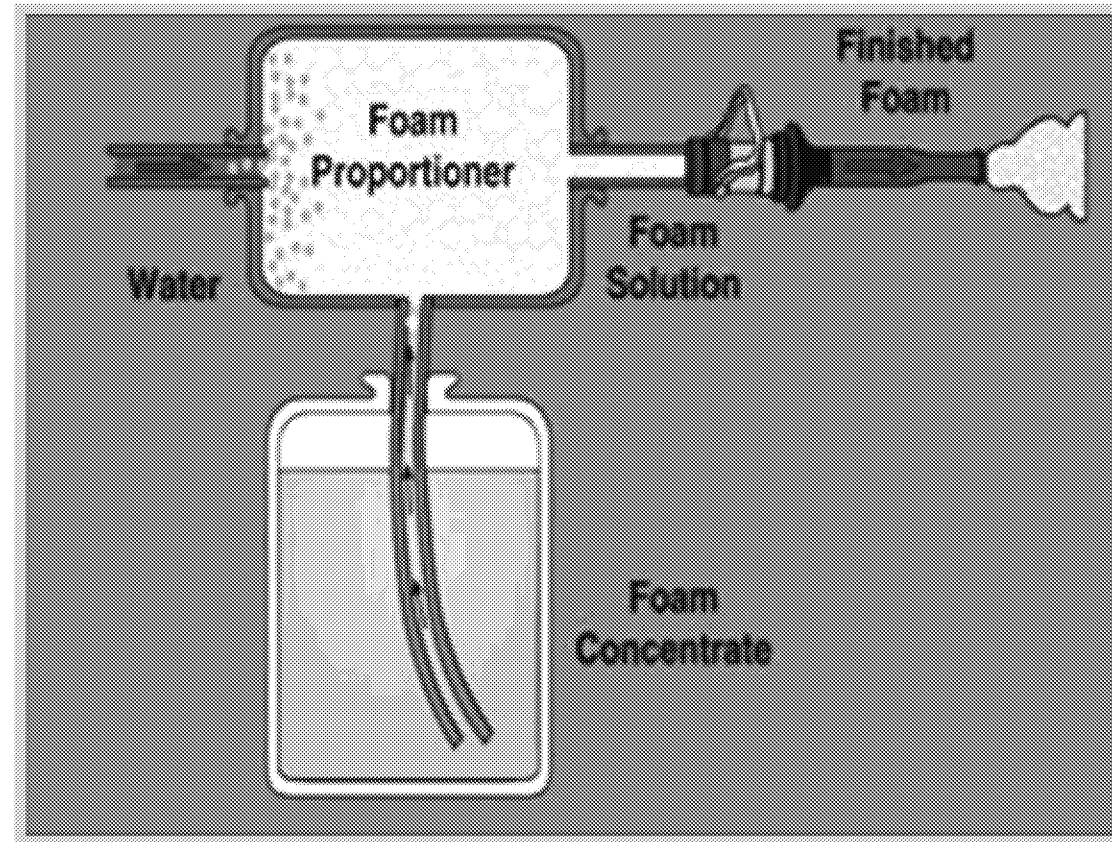
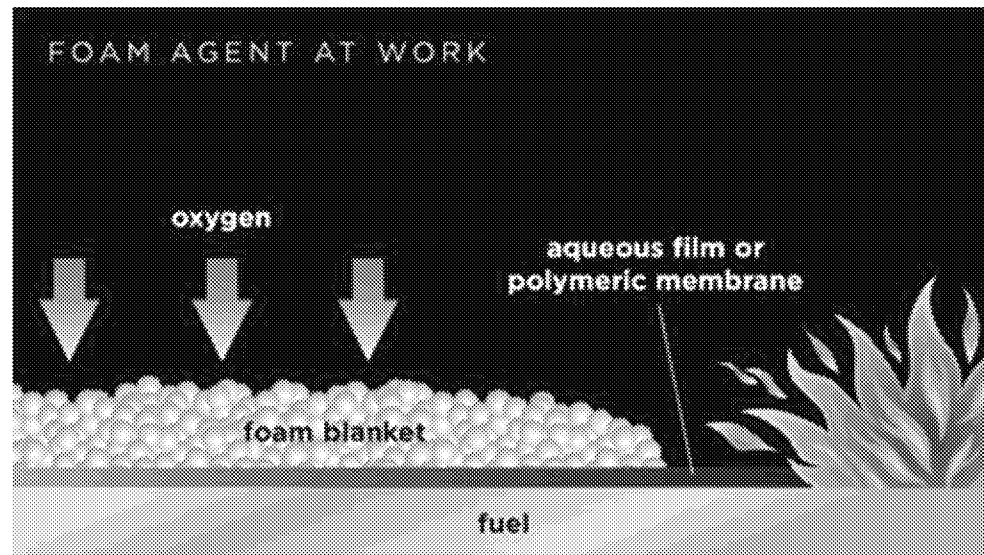
PART-4

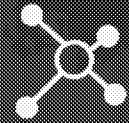
UNDERSTANDING PUBLIC HEALTH IMPLICATIONS OF PFAS EXPOSURE IN REPRODUCTIVE AGED COUPLES

AFFF Mechanism of Action

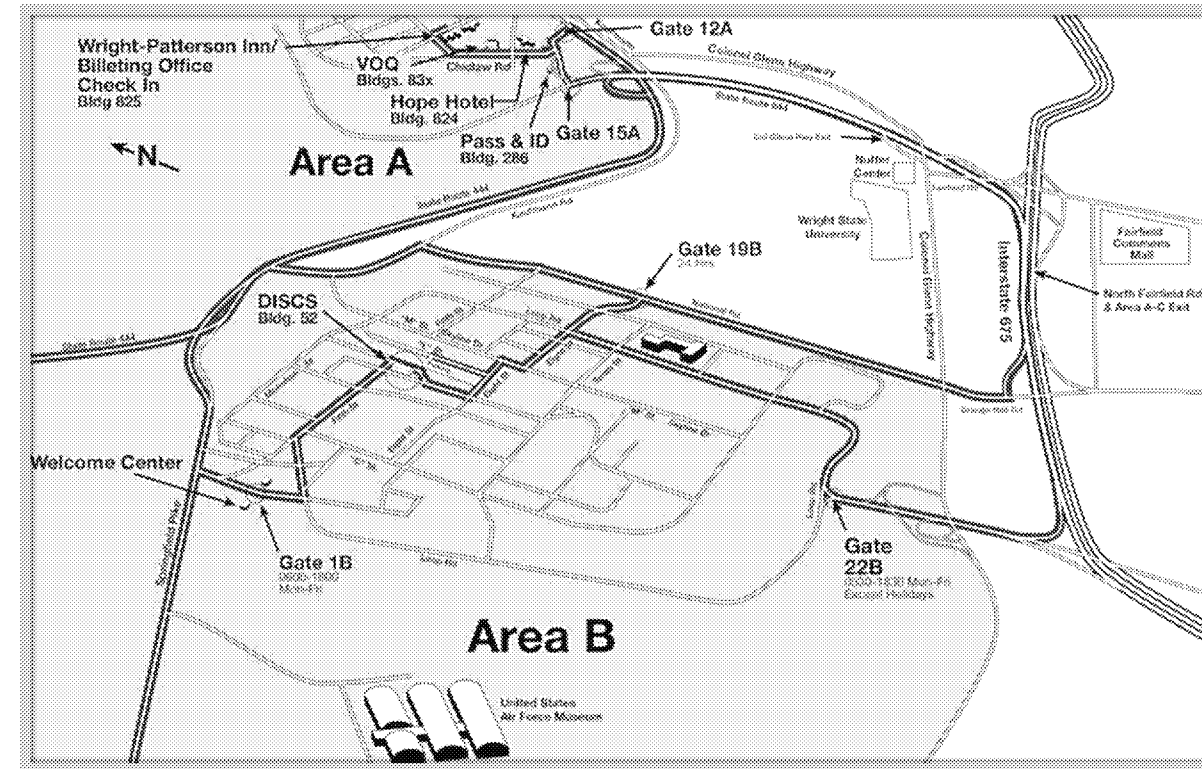


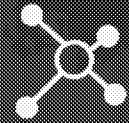
AFFF HAS BEEN USED BY THE AIR FORCE
SINCE THE 1970s





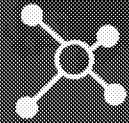
- ✓ OH EPA Director shut down two wells in Area A of Wright Patt and required monthly testing of other wells to detect potential contamination
- ✓ Levels exceeded the new EPA lifetime exposure standard of 70 parts per trillion





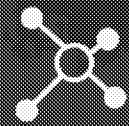
- ✓ The Air Force awarded a \$6.2 million contract to ICL Performance Products in August 2015 for 418,000 gallons of Phos-Chek 3 percent.
- ✓ Phos-Chek 3 percent was marketed as an environmentally responsible foam; it is a 6 carbon chain AFFF developed under the EPA's Stewardship Program
- ✓ Delivery of the product began in August 2016, and all foam in fire stations was replaced by 2017
- ✓ Regrettable substitution



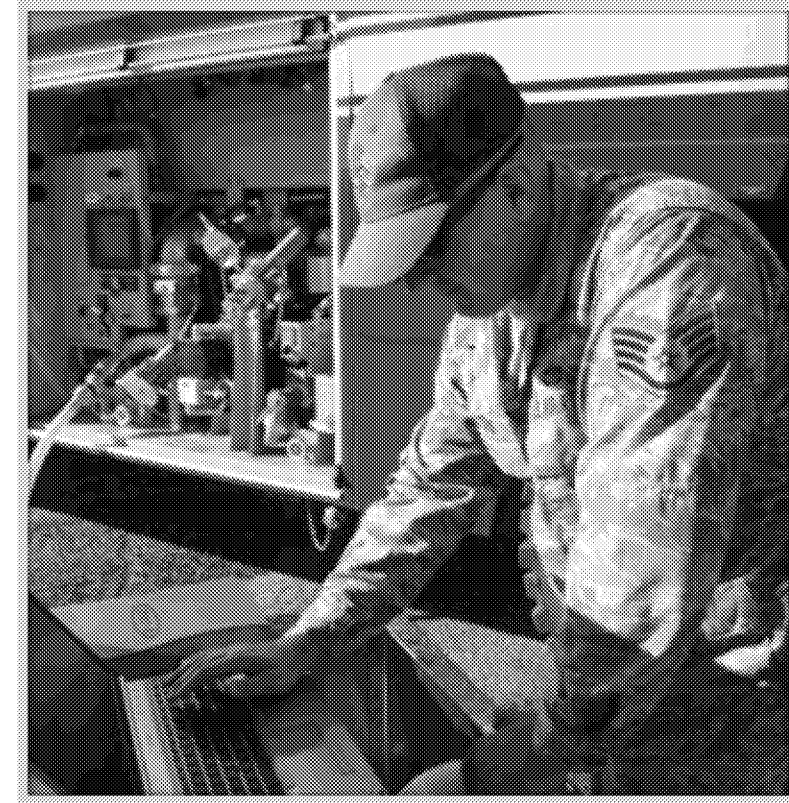


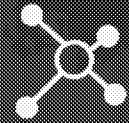
- ✓ The Air Force was also awarded a contract to retrofit all aircraft rescue and firefighting vehicles (>800) with a mobile foam test system
- ✓ Fire vehicle operational checks and required annual foam tests will be performed without discharging AFFF into the environment
- ✓ Retrofitting will be complete in 2018
- ✓ Viable strategy





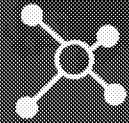
THE AIR FORCE DISCONTINUED REGULAR FOAM DISCHARGE TESTS
IN JULY 2015



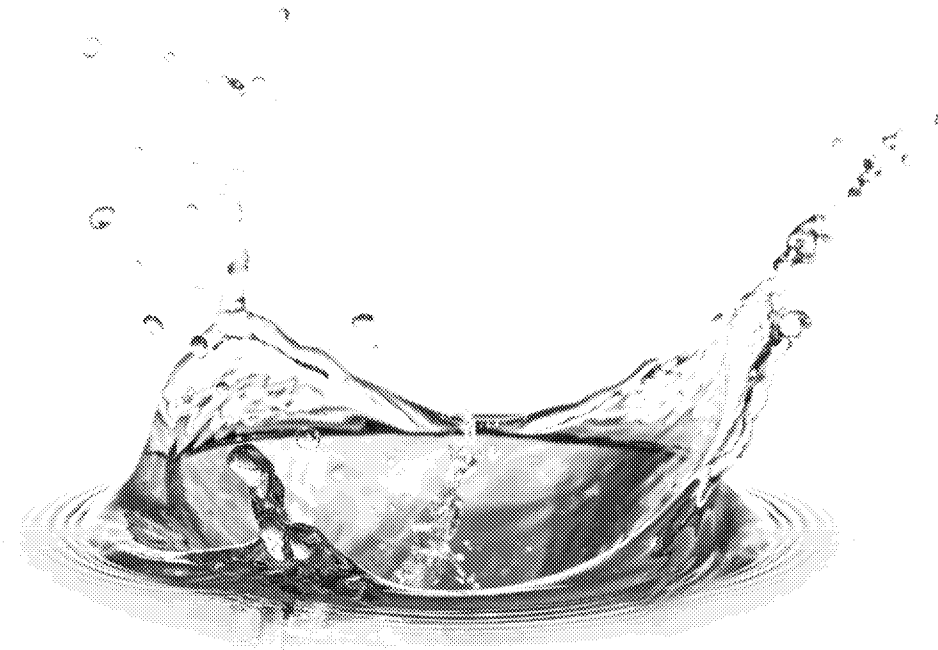


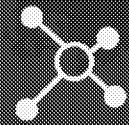
- ✓ The Air Force has restricted AFFF for emergency use only.
- ✓ When AFFF is used, Air Force hazardous materials teams will treat the response scene as a hazardous site, and remove/destroy foam residue before contamination can occur
 - Training exercises performed in double lined pits to prevent soil and groundwater contamination
 - Tanks and ponds to collect burn pit effluent
 - Incineration disposal facilities
- ✓ Viable strategy

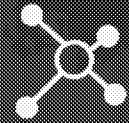




- ✓ **Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA)**
 - Assess, Inspect, Investigate, Clean-up
- ✓ **If lifetime EPA limit is exceeded due to the Air Force mission, the Air Force will provide alternative drinking water sources**
 - Bottled water
 - Water filtration systems
 - Connecting private wells to public drinking water supplies







- ✓ PFAS/PFOA exposure was believed to have contributed to this couples' infertility, with emphasis on potential male factor causes
- ✓ Infertility affects 15% of couples
- ✓ Male factor infertility is diagnosed in 20-30% of couples seeking treatment
- ✓ Air Force initiatives may decrease future occupational exposures
- ✓ More occupational based research in high risk populations such as military and civilian firefighters is needed
- ✓ Understanding how environmental chemicals like PFAS increases the risk of infertility and pregnancy loss is a research gap and public health goal

